

What Are the Optimal Dose of Administration and Time of Drainage for Topical Tranexamic Acid in Patients Undergoing Cardiac Surgery?

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Despite technological advances in cardiac surgery, bleeding and blood transfusion during cardiac operations are still among the most important challenges facing cardiac surgeons. In recent years, the use of antifibrinolytic agents such as tranexamic acid (TXA) in patients undergoing cardiac surgery has been remarkably effective in reducing blood loss and the need for blood transfusions. TXA, in an intravenous form, has a class IA recommendation for preventing blood loss and decreasing the need for blood transfusion and reexploration. However, the associated postoperative complications have limited its applicability [1].

To reduce postoperative complications such as seizure, thromboembolism, and early graft occlusion, many cardiac surgeons use the topical form of TXA instead of the systemic intravenous form, or they use a combination of these two forms. However, the optimal dose, time of administration, and time of drainage required to reduce blood loss and the need of blood transfusion, as well as avoid postoperative complications, have yet to be determined.

There is considerable diversity among published studies regarding the dose, time of topical TXA administration, and drainage time, as the basis of the dosage used in those studies is unknown. For example, Nouraei et al. diluted 2 g of TXA in 500 mL of saline at 37°C and poured it into the pericardial cavity. The solution was removed 5 minutes before the sternotomy closure. According to Nouraei et al.

[2], topical TXA, in addition to significantly reducing blood loss and the frequency of blood transfusions, did not cause any complications such as mortality, myocardial infarction, cerebrovascular accident, seizure, reexploration, or renal failure in patients undergoing cardiac surgery. Patel et al. [3] administered 20 mg/kg of TXA intravenously after sternotomy, as well as another 50 mg/kg of TXA in 20 mL of saline intrapericardially before sternal closure, and let it remain for 20 minutes before drainage. They reported that simultaneously using intravenous and topical TXA reduced blood loss and the frequency of transfusions [3]. Taksaudom et al. [4] dissolved 1 g of TXA in 100 mL of normal saline and administered it intrapericardially during sternal closure in patients undergoing on-pump cardiac surgery. They reported no significant difference in postoperative bleeding or the frequency of blood transfusions between the patients who received TXA and those who did not [4]. Kimenai et al. [5] administered 2 g of TXA intravenously before making the sternal incision and 2 g of TXA diluted in 200 mL of saline intrapericardially before sternal closure, as well as 2 g of TXA after surgery. They found no difference in postoperative blood loss depending on whether TXA was administered [5]. Ali Shah et al. [6] poured a solution of 2.5 g of TXA in 250 mL of normal saline into the pericardial cavity before sternal closure and found a significant decrease in mean volume of postoperative bleeding. Table 1 summarizes the various dosages

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Table 1. Various reported dosages of tranexamic acid, drainage times, and outcomes

Author [reference] (year)	Dosage	Drainage time	Outcomes
Nouraei et al. [2] (2013)	2 g in 500 mL of saline	5 min before sternal closure	Reduction in blood loss and frequency of transfusions
Patel et al. [3] (2017)	50 mg/kg in 20 mL of saline	20 min before sternal closure	Reduction in blood loss and frequency of transfusions
Taksaudom et al. [4] (2017)	1 g in 100 mL of saline	Before sternal closure until the patient was moved to the intensive care unit ^{a)}	No significant difference in postoperative bleeding or frequency of blood transfusions
Kimenai et al. [5] (2016)	2 g in 200 mL of saline	1 min before sternal closure	No difference in postoperative bleeding or frequency of blood transfusions
Ali Shah et al. [6] (2016)	2.5 g in 250 mL of saline	Before sternal closure ^{a)}	Significant decrease in mean volume of postoperative bleeding

^{a)}The exact time of drainage of topical tranexamic acid was not reported.

and outcomes of TXA use in these and other studies.

As shown above, studies have reported various TXA doses with heterogeneous results. There is much debate in the literature regarding the clinical efficacy of lower doses of TXA, due to the absence of evidence that it improves patient safety at doses of less than 50 mg/kg in terms of reducing the rates of blood transfusion or surgical reexploration [7].

Regarding the positive outcomes of topical TXA in reducing blood loss and the need for blood transfusions in patients undergoing cardiac surgery, further well-designed controlled trials should be conducted to determine the optimal dose and time of administration as well as the time of drainage from the mediastinum cavity. It would also be important for future clinical trials involving topical TXA in cardiac surgery to determine the basis for the dosage calculation and the time of drainage. Since the current literature does not adequately discuss the safety and side effects of topical TXA, further large, prospective, blinded studies are warranted to establish the safety of various doses of TXA in patient undergoing cardiac surgery. Therefore, future studies should consider the pharmacetics and pharmacokinetics of TXA in order to appropriately adjust the intrapericardial dosage. In addition, there is a critical need for a thorough literature review to be conducted to synthesize the results of all the pertinent studies.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

References

1. Dhir A. *Antifibrinolytics in cardiac surgery*. Ann Card Anaesth 2013;16:117-25.
2. Nouraei M, Baradari AG, Ghafari R, Habibi MR, Zeydi AE, Sharifi N. *Decreasing blood loss and the need for transfusion after CABG surgery: a double-blind randomized clinical trial of topical tranexamic acid*. Turk J Med Sci 2013;43:273-8.
3. Patel J, Prajapati M, Patel H, Gandhi H, Deodhar S, Pandya H. *Topical and low-dose intravenous tranexamic acid in cyanotic cardiac surgery*. Asian Cardiovasc Thorac Ann 2017;25:118-22.
4. Taksaudom N, Siwachat S, Tantraworasin A. *Additional effects of topical tranexamic acid in on-pump cardiac surgery*. Asian Cardiovasc Thorac Ann 2017;25:24-30.
5. Kimenai DM, Gerritse BM, Lucas C, et al. *Effectiveness of pericardial lavage with or without tranexamic acid in cardiac surgery patients receiving intravenous tranexamic acid: a randomized controlled trial*. Eur J Cardiothorac Surg 2016;50:1124-31.
6. Ali Shah MU, Asghar MI, Siddiqi R, Chaudhri MS, Janjua AM, Iqbal A. *Topical application of tranexamic acid reduces postoperative bleeding in open-heart surgery: myth or fact?* J Coll Physicians Surg Pak 2015;25:161-5.
7. Gofton TE, Chu MW, Norton L, et al. *A prospective observational study of seizures after cardiac surgery using continuous EEG monitoring*. Neurocrit Care 2014;21:220-7.